

# STM - Structure Search

11/15/07

10/583,803

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L4 ANSWER 1 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2006:847858 CAPLUS  
 DOCUMENT NUMBER: 145:278405  
 TITLE: Drugs with improved hydrophobicity for incorporation  
 in medical devices  
 INVENTOR(S): Desai, Neil P.; Tao, Chunlin; Yu, Chengzhi; Wang,  
 Qinwei; Soon-Shiong, Patrick  
 PATENT ASSIGNEE(S): American Bioscience, Inc., USA  
 SOURCE: PCT Int. Appl., 43pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006089207	A2	20060824	WO 2006-US5799	20060221
WO 2006089207	A3	20070518		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA AU 2006214100 A1 20060824 AU 2006-214100 20060221 CA 2598213 A1 20060824 CA 2006-2598213 20060221 PRIORITY APPLN. INFO.: US 2005-654175P P 20050218 WO 2006-US5799 W 20060221				

OTHER SOURCE(S): MARPAT 145:278405

AB The invention provides a medical device comprising a hydrophobic analog of a medicament known to inhibit cell proliferation and migration. The invention also provides a method of treating a narrowing in a body passageway comprising placing an implantable medical device comprising a hydrophobic analog of a medicament known to inhibit cell proliferation and migration. The medicaments can be incorporated within or coated on the device. The invention further provides hydrophobic analogs of medicaments known to inhibit cell proliferation and migration.

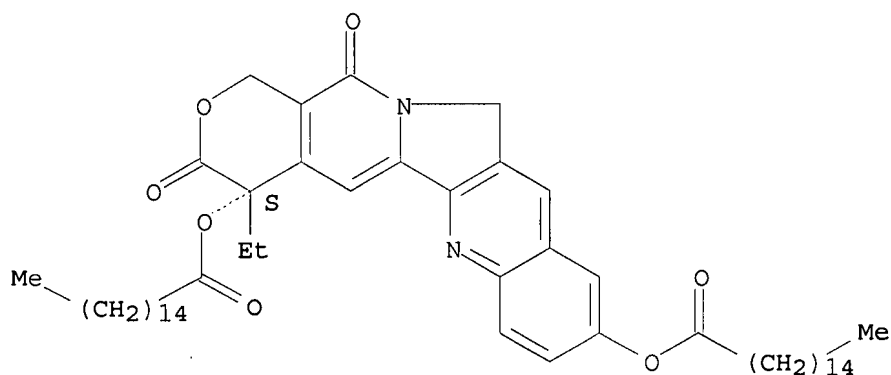
IT 848078-09-1P 848078-11-5P 857892-69-4P  
 857892-70-7P 857892-71-8P 857892-72-9P  
 857892-73-0P 857892-77-4P 857892-80-9P  
 857892-81-0P 857892-82-1P 857892-83-2P  
 906649-23-8P 906649-24-9P

RL: PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drugs with improved hydrophobicity for incorporation in medical devices)

RN 848078-09-1 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,  
 4-ethyl-4,9-bis(1-oxopropoxy)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2006:620137 CAPLUS  
 DOCUMENT NUMBER: 145:230786  
 TITLE: Preparation of precursors hydroxycamptothecine ester and its derivative as antitumor agent  
 INVENTOR(S): Lu, Wei; He, Xungui; Zhang, Xiongwen; Ding, Jian  
 PATENT ASSIGNEE(S): Shanghai Inst. of Medicament, Chinese Academy of Sciences, Peop. Rep. China  
 SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 12 pp.  
 CODEN: CNXXEV  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Chinese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

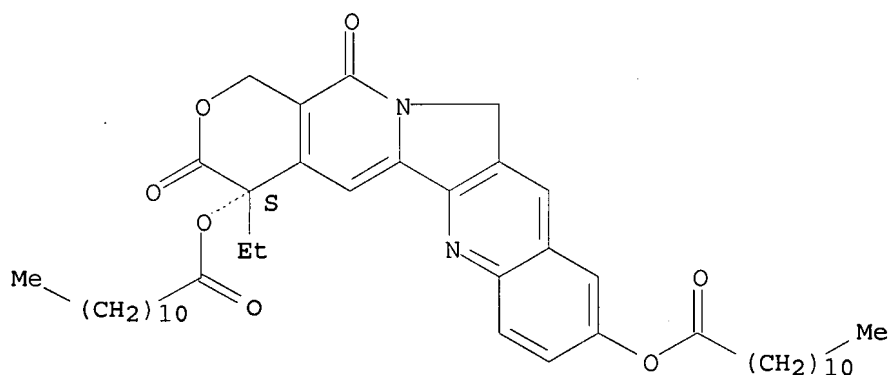
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CN 1673226	A	20050928	CN 2004-10017128	20040323
PRIORITY APPLN. INFO.:			CN 2004-10017128	20040323
OTHER SOURCE(S):	CASREACT 145:230786; MARPAT 145:230786			
GI				

10/583,803

RN 905564-83-2 CAPLUS

CN Dodecanoic acid, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI) (CA INDEX NAME)

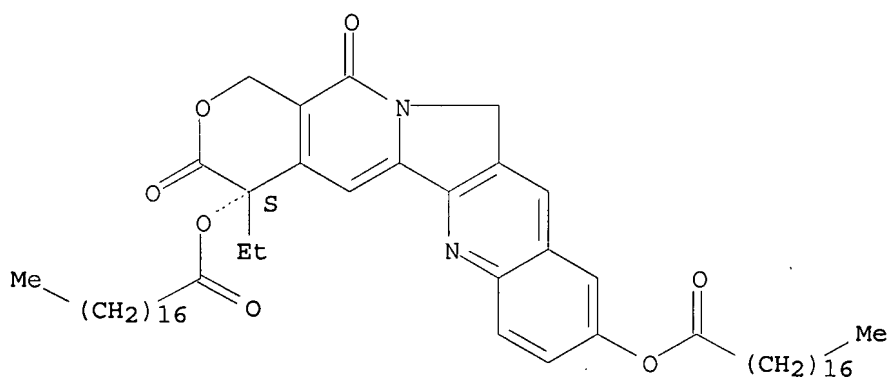
Absolute stereochemistry.



RN 905564-84-3 CAPLUS

CN Octadecanoic acid, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 3 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:296608 CAPLUS

DOCUMENT NUMBER: 144:357695

TITLE: Preparation of parenteral solutions of poorly water soluble drugs using dimethyl isosorbide

INVENTOR(S): Desai, Neil P.; Tao, Chunlin; Yang, Andrew; Beals Grim, Bridget; De, Tapas; Soon-Shiong, Patrick

PATENT ASSIGNEE(S): American Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 18 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006034147	A2	20060330	WO 2005-US33396	20050916

10/583,803

WO 2006034147

A3

20061214

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

US 2004-610407P

P 20040916

AB Sterile, stable, parenteral formulations of poorly water-soluble drugs dissolved in di-Me isosorbide (DMI), a water-miscible solvent, as well as methods for their preparation and administration are described. For example, an aqueous solution of cyclosporine A was prepared containing cyclosporine A 2.8 weight%,

DMI 57.6 volume%, and water 42.4 volume%.

IT 848078-11-5 857892-69-4

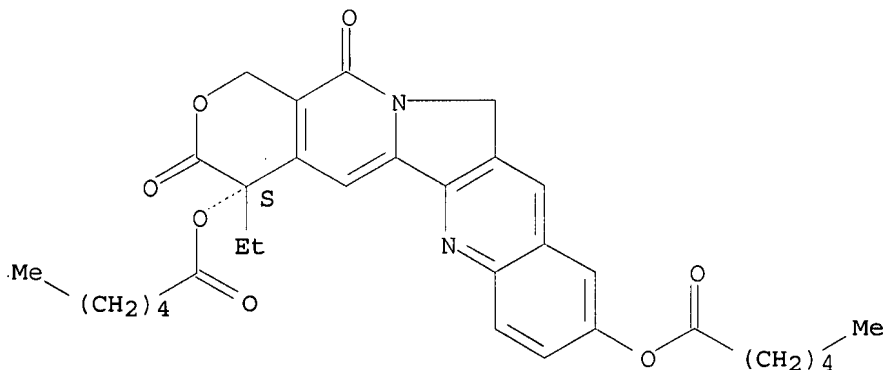
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of parenteral solns. of poorly water soluble drugs using di-Me isosorbide)

RN 848078-11-5 CAPLUS

CN Hexanoic acid, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI) (CA INDEX NAME)

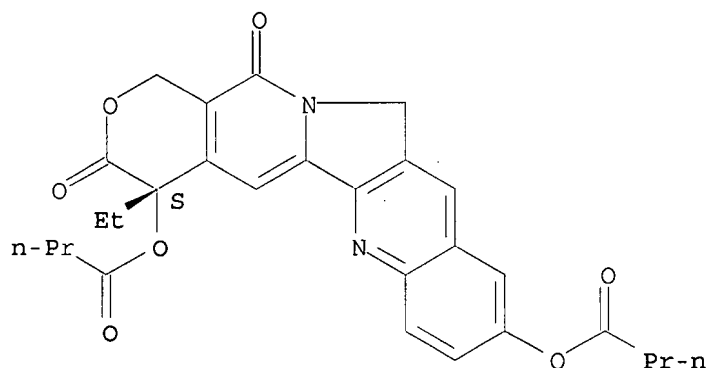
Absolute stereochemistry.



RN 857892-69-4 CAPLUS

CN Butanoic acid, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:180167 CAPLUS

DOCUMENT NUMBER: 144:391205

TITLE: Copper-free Sonogashira reaction using 7-chloro camptothecins

AUTHOR(S): Luo, Yu; Gao, Heyong; Li, Yunfei; Huang, Weigang; Lu, Wei; Zhang, Zhaoguo

CORPORATE SOURCE: Shanghai Institute of Materia Medica, SIBS, Chinese Academy of Sciences, Graduate School of the Chinese Academy of Sciences, Shanghai, 201203, Peop. Rep. China

SOURCE: Tetrahedron (2006), 62(11), 2465-2470

CODEN: TETRAB; ISSN: 0040-4020

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:391205

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB We studied copper-free Sonogashira reaction using 7-chlorocamptothecins I (R1 = H, OAc), and determined that rac-BINAP/Pd(OAc)<sub>2</sub> was an efficient catalyst for the coupling reaction. With this process, a number of 7-substituted camptothecins II [R1 = H, OAc; R2 = cyclopentyl, Ph, SiMe<sub>3</sub>, 2-hydroxyisopropyl] with a wide range of functional groups are potentially accessible. Besides, two drugs, SN-38 (III) and BNP-1350 (IV), could be prepared by this method.

IT 882737-92-0P

RL: PNU (Preparation, unclassified); PREP (Preparation)

(copper-free Sonogashira coupling reaction of 7-chlorocamptothecins with alkynes)

RN 882737-92-0 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-4-ethyl-11-(3-hydroxy-3-methyl-1-butynyl)-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

10/583,803

IT 882737-86-2P

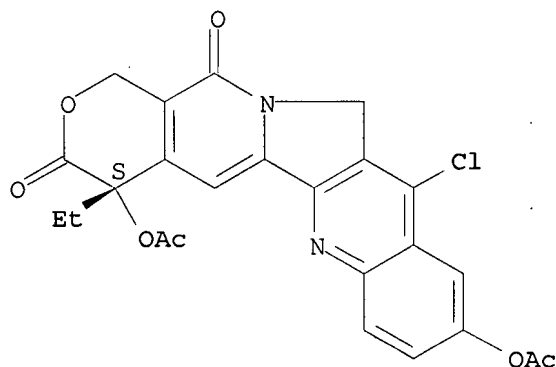
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and Sonogashira coupling reaction of, with acetylene derivs.; copper-free Sonogashira coupling reaction of 7-chlorocamptothecins with alkynes)

RN 882737-86-2 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-11-chloro-4-ethyl-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



IT 882737-90-8P

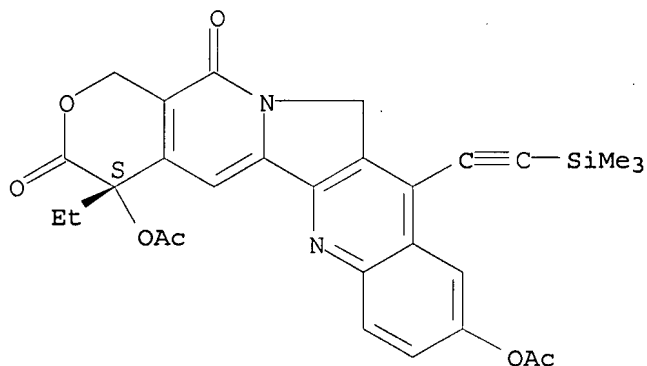
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation, desilylation, hydrogenation and O-deacetylation of; copper-free Sonogashira coupling reaction of 7-chlorocamptothecins with alkynes)

RN 882737-90-8 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-4-ethyl-11-[(trimethylsilyl)ethynyl]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

37

THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:1084194 CAPLUS

DOCUMENT NUMBER: 144:362547

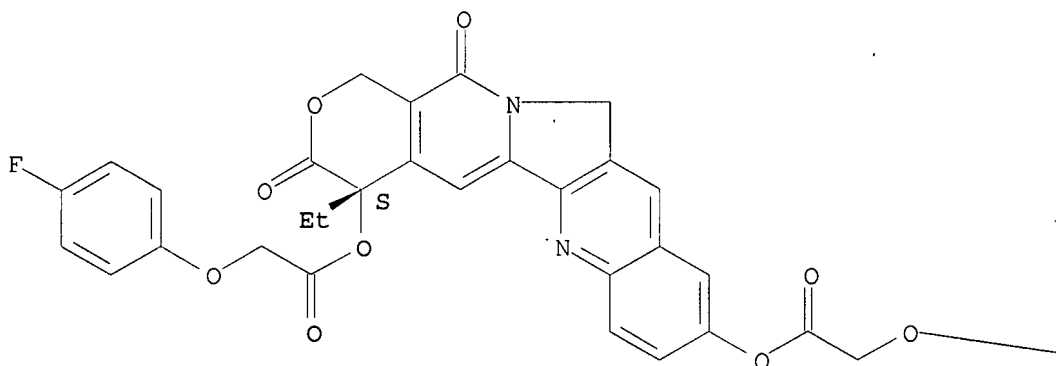
TITLE: Synthesis and antitumor activity of 20-O-linked camptothecin ester derivatives

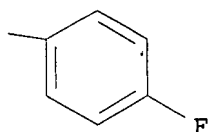
10/583,803

AUTHOR(S): Pan, Xiandao; Liu, Hongyan; Sun, Piaoyang; Zhu, Chenggen; Yang, Jing; Yuan, Kaihong; Han, Rui  
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050, Peop. Rep. China  
SOURCE: Yaoxue Xuebao (2004), 39(8), 591-597  
CODEN: YHHPAL; ISSN: 0513-4870  
PUBLISHER: Yaoxue Xuebao Bianjibu  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 144:362547  
AB To improve the profile of 20 (S)-camptothecin, a series of 20-O-linked camptothecin phenoxyacetic acid ester derivs. have been designed. These derivs. were synthesized by the method of acylation. Their chemical structures were confirmed with <sup>1</sup>HNMR, IR, MS, and HRMS. The cytotoxicities of the compds. were tested by MIT assay. The in vivo antitumor activities of these esters were evaluated against mouse liver tumor H22 in mice. Twelve derivs. of camptothecin ester are new compds. In vitro and in vivo antitumor activity has indicated that some derivs. appeared significantly more effective than topotecan in the H22 mouse liver tumoral model.  
IT 634586-91-7P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(antitumor activity of 20-O-linked camptothecin ester derivs.)  
RN 634586-91-7 CAPLUS  
CN Acetic acid, (4-fluorophenoxy)-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:612008 CAPLUS

DOCUMENT NUMBER: 143:120555

TITLE: Preparation of di-ester derivatives of camptothecins for cancer treatment

INVENTOR(S): Cao, Zhi-Song; Tao, Chunlin

PATENT ASSIGNEE(S): American Bioscience, Inc., USA

SOURCE: PCT Int. Appl., 14 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005062991	A2	20050714	WO 2004-US43978	20041223
WO 2005062991	A3	20050929		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-531941P P 20031223

OTHER SOURCE(S): MARPAT 143:120555

AB The present invention is related to lower alkyl 10,20-di-O-ester derivs. of camptothecins and pharmaceutical formulations thereof for treatment of cancers. A method for inhibition of the enzyme topoisomerase I by contacting the enzyme with the alkyl 10,20-di-O-esters of camptothecins is also described. The compds. and pharmaceutical formulations of the present invention possess increased biol. life span and bioavailability and reduced toxicity, while maintaining anti-cancer activity. Thus, 10-hydroxycamptothecin-10,20-dipropionate was prepared by the reaction of



10/583,803

1.0 g of 10-hydroxycamptothecin and 20 mL of propionic anhydride in a 81% yield. 10-Hydroxycamptothecin-10,20-dipropionate showed the in vitro growth inhibition of MX-1 (human breast carcinoma) cells at IC50 of 46.2  $\mu$ M. Nanoparticles of 10-hydroxycamptothecin-10,20-dipropionate (30 mg) were prepared by sonication with human serum albumin and lyophilized. The resulting cake could be easily reconstituted to the original dispersion by addition of sterile water or saline. The particle size after reconstitution was the same as before lyophilization (50 to 220 nm).

IT 19685-12-2P 848078-09-1P

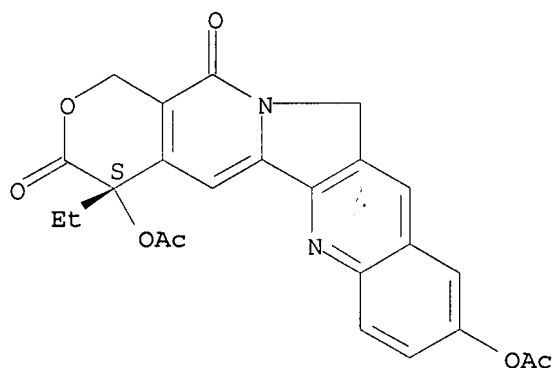
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and nanoparticle formulation of camptothecin 10,20-di-ester prodrugs for cancer treatment)

RN 19685-12-2 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-4-ethyl-, (4S)- (9CI) (CA INDEX NAME)

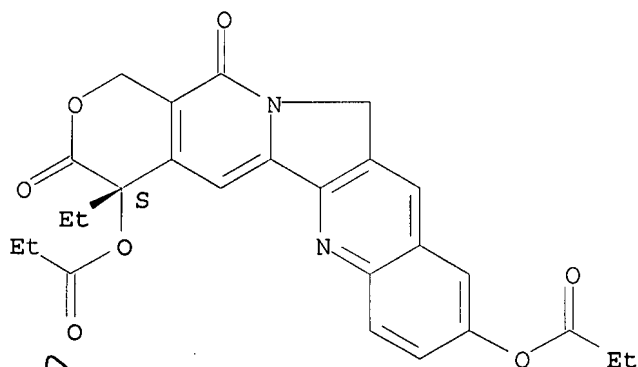
Absolute stereochemistry.



RN 848078-09-1 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4,9-bis(1-oxopropoxy)-, (4S)- (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2005:612006 CAPLUS

DOCUMENT NUMBER: 143:120554

TITLE: Preparation of camptothecin di-ester prodrugs for cancer treatment

INVENTOR(S): Soon-Shiong, Patrick; Desai, Neil P.; Tao, Chunlin;

PATENT ASSIGNEE(S): Yu, Chengzhi  
 SOURCE: American Bioscience, Inc., USA  
 PCT Int. Appl., 37 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005062985	A2	20050714	WO 2004-US43719	20041223
WO 2005062985	A3	20050909		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2007161668	A1	20070712	US 2007-583803	20070123
PRIORITY APPLN. INFO.:			US 2003-532231P	P 20031223
			WO 2004-US43719	W 20041223

OTHER SOURCE(S): CASREACT 143:120554; MARPAT 143:120554

AB The present invention is related to 10,20-di-O ester derivs. of  
 camptothecin and pharmaceutical formulations thereof. The compds. and  
 pharmaceutical formulations of the present invention possess increased  
 biol. life span and bioavailability and reduced toxicity, while  
 maintaining anti-cancer activity. Thus, camptothecin 10,20-di-O-hexonate  
 (CY4) was prepared by the reaction of 10-hydroxycamptothecin (1.8 g, 4.94  
 mmol) and hexanoic anhydride (50 mL) at 100° in a 86% yield. The  
 CY4 compound showed the in vitro growth inhibition of MX-1 (human breast  
 carcinoma) cells at IC50 of 7.8 µM. Nanoparticles of CY4 (20 mg) were  
 prepared by sonication with human serum albumin and lyophilized without  
 adding any cryoprotectant. The resulting cake could be easily  
 reconstituted to the original dispersion by addition of sterile water or  
 saline. The particle size after reconstitution was the same as before  
 lyophilization (350 to 420 nm).

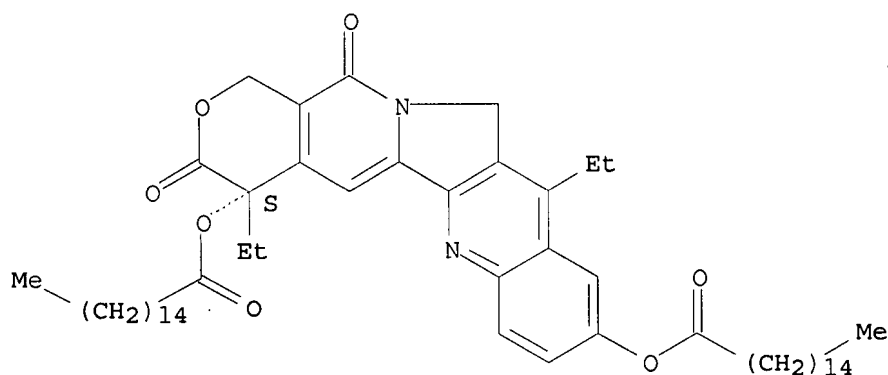
IT 857892-71-8P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic  
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP  
 (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (preparation and nanoparticle formulation of camptothecin di-ester prodrugs  
 for cancer treatment)

RN 857892-71-8 CAPLUS

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (4S)-4-ethyl-3,4,12,14-  
 tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-  
 diyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 8 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
 ACCESSION NUMBER: 2005:394830 CAPLUS  
 DOCUMENT NUMBER: 142:435789  
 TITLE: Preparation of tocopherol-modified pharmaceuticals  
 INVENTOR(S): Zhang, Yuehua; Gold, Lynn C.  
 PATENT ASSIGNEE(S): Sonus Pharmaceuticals, Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 42 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005096340	A1	20050505	US 2004-978222	20041029
US 7223770	B2	20070529		
AU 2004285037	A1	20050512	AU 2004-285037	20041029
CA 2543722	A1	20050512	CA 2004-2543722	20041029
WO 2005042539	A1	20050512	WO 2004-US36127	20041029
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SI, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1682552	A1	20060726	EP 2004-817489	20041029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1875022	A	20061206	CN 2004-80032084	20041029
BR 2004015858	A	20070109	BR 2004-15858	20041029
JP 2007509978	T	20070419	JP 2006-538354	20041029
MX 2006PA04429	A	20061211	MX 2006-PA4429	20060421
IN 2006KN01255	A	20070427	IN 2006-KN1255	20060512
US 2006229359	A1	20061012	US 2006-450795	20060608
US 2007207196	A1	20070906	US 2007-690005	20070322
PRIORITY APPLN. INFO.:				
			US 2003-515364P	P 20031029
			US 2004-556137P	P 20040324
			US 2004-558762P	P 20040401
			US 2004-621655P	P 20041026
			US 2004-978222	A1 20041029

AB Tocopherol-modified pharmaceuticals, emulsions, microemulsions, and micelle formulations that include the above drugs, methods for making the compds. and formulations, methods for administering the compds. and formulations; and methods for treating conditions using the compds. and formulations are disclosed. Thus, tocopherol succinate 7-ethyl-10-hydroxycamptothecin was prepared starting from 7-ethyl-10-hydroxycamptothecin. An emulsion contained the above drug 0.69, vitamin E 7.31, TPGS 5, Poloxamer-407 1, and saline 86%.

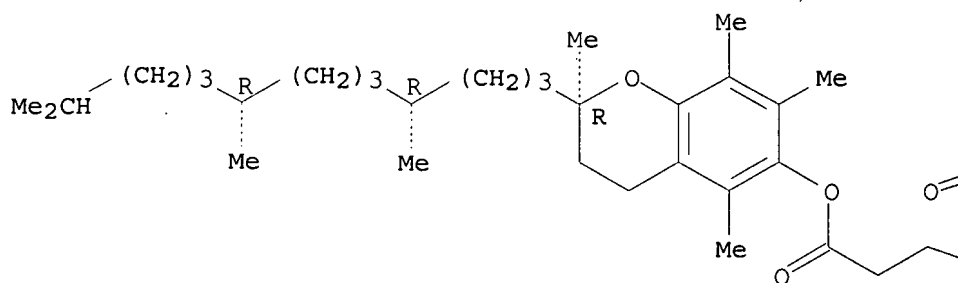
IT 850655-06-0P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of tocopherol-modified pharmaceuticals)

RN 850655-06-0 CAPLUS

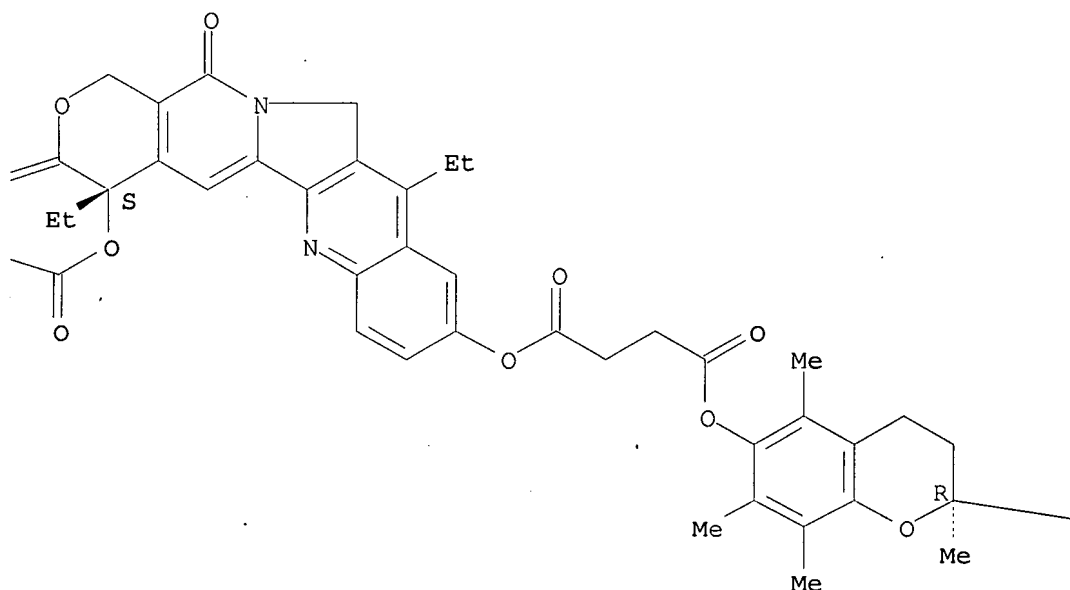
CN Butanedioic acid, (4S)-4,11-diethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl bis[(2R)-3,4-dihydro-2,5,7,8-tetramethyl-2-[(4R,8R)-4,8,12-trimethyltridecyl]-2H-1-benzopyran-6-yl] ester (9CI) (CA INDEX NAME)

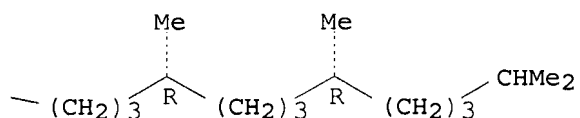
Absolute stereochemistry.

PAGE 1-A



PAGE 1-B





L4 ANSWER 9 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:905775 CAPLUS

DOCUMENT NUMBER: 141:380058

TITLE: Hydroxy-substituted 20-acyloxycamptothecin polymer derivatives and use of the same for the manufacture of an antiproliferative medicament

PATENT ASSIGNEE(S): Debio Recherche Pharmaceutique S.A., Switz.

SOURCE: PCT Int. Appl., 43 pp.

CODEN: PIXXD2

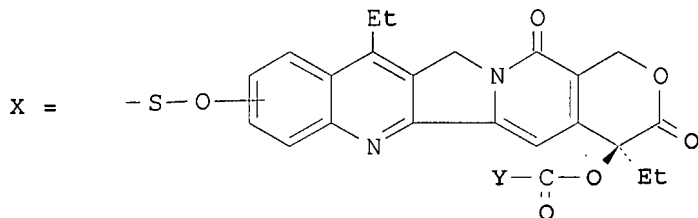
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004092205	A1	20041028	WO 2003-IB1430	20030416
W: CH				
PRIORITY APPLN. INFO.: GI			WO 2003-IB1430	20030416



AB The present invention relates to pharmacol. active hydroxy-substituted 20-acyloxy-7-ethylcamptothecin polymer derivs.,  $X_1C(:O)O(CH_2CH_2O)_n(C(:O)X_2)$  [I;  $n = 10 - 1000$ ; when  $X_1 = (\text{un})\text{branched C1-6-alkyl}$  then  $C(:O)$  is

missing; or X1, X2 = X; Y = Me(CH<sub>2</sub>)<sub>m</sub>; m = 1 - 18; S = peptide spacer {e.g., Gly-Leu-Phe-Gly, Gly-Phe-Leu-Gly, Gly-Phe-Phe-Ala, Gly-Phe-Phe-Leu, Gly-Phe-Tyr-Ala, Ala-Gly-Val-Phe, Gly-Leu-Ala, Gly-Leu-Gly, Gly-Phe-Gly, Gly-Phe-Ala, D-Ala-Phe-Lys, D-Val-Leu-Lys, Lys-Gly-Leu-Phe-Gly (with at least one of α- and ε-amino of Lys being linked through a carbamate bond or linked with an aliphatic diamine through a carbamate bond)}], which have antiproliferative cell activity and are water-soluble. Thus, H-Gly-Leu-Phe-Gly-OH is treated with 10 kD polyethylene glycol monomethyl ether benzotriazolyl carbonate, and then coupled with 7-ethyl-10-hydroxycamptothecin 20-O-propionate to give the tethered alkaloid I [X1 = Me (with no C:O next to it), X2 = X, Y = Et, S = Gly-Leu-Phe-Gly, PEG = 10 kD]. The latter was tested for pharmacol. activity [T/C = 130% at 50 mg/kg and 164% at 100 mg/kg in mice injected with P388/VCR cells].

IT 781640-44-6DP, 10 kD PEG

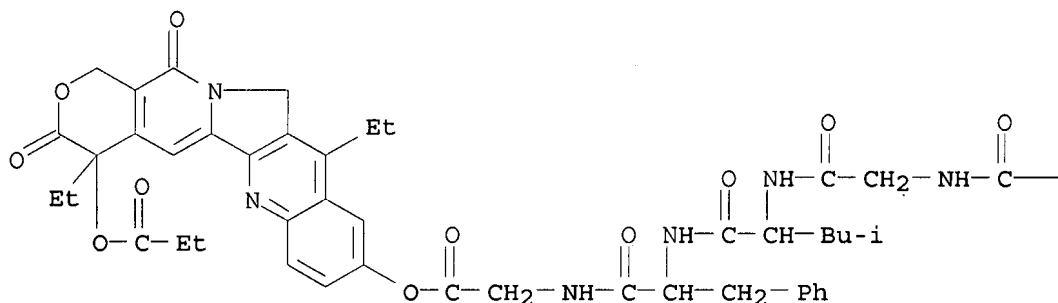
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

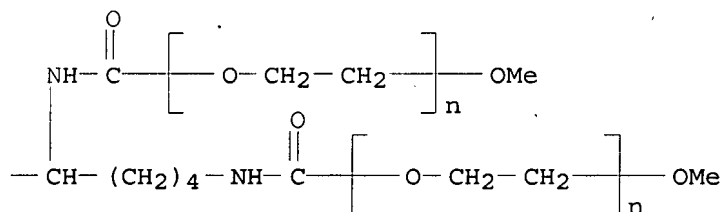
RN 781640-44-6 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, diester with N2,N6-dicarboxy-L-lysylglycyl-L-leucyl-L-phenylalanylglycine 5-[(4S)-4,11-diethyl-3,4,12,14-tetrahydro-3,14-dioxo-4-(1-oxopropoxy)-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-9-yl] ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 1-B



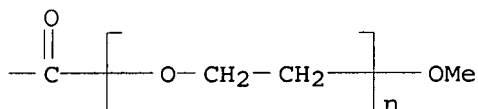
IT 781640-41-3DP, 10 kD PEG 781640-43-5DP, 10 kD PEG

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(hydroxy-substituted 20-acyloxycamptothecin polymer derivs. and use thereof for the manufacture of an antiproliferative medicament)

RN 781640-41-3 CAPLUS

CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-methoxy-, ester with N-carboxyglycyl-L-leucylglycine 3-(4S)-4,11-diethyl-3,4,12,14-tetrahydro-3,14-dioxo-4-(1-oxopropoxy)-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:884286 CAPLUS

DOCUMENT NUMBER: 142:316991

TITLE: Preparation of camptothecin carbonates and esters with enhanced antitumor activity

INVENTOR(S): Lu, Wei; Zhu, Qin; Pan, Junfang; Cai, Junchao; Ding, Jian

PATENT ASSIGNEE(S): Shanghai Institute of Pharmacy, Chinese Academy of Sciences, Peop. Rep. China; Huatuo Medical Science and Technology Development Co., Ltd.

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.  
CODEN: CNXXEV

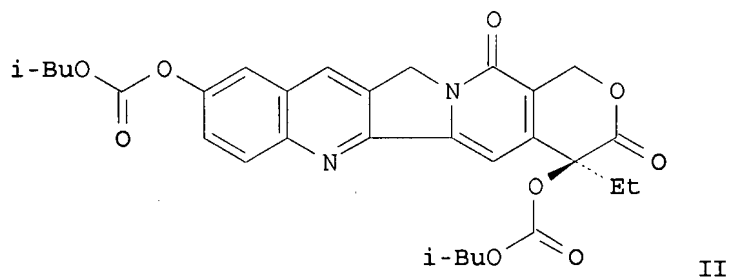
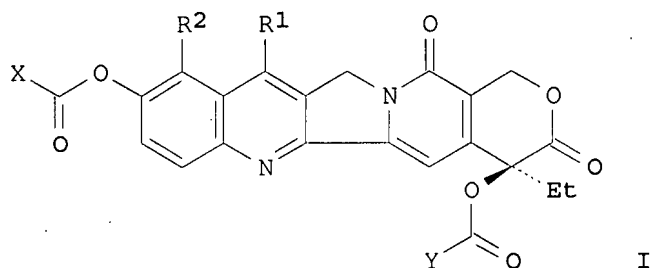
DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CN 1465577	A	20040107	CN 2002-112268	20020627
PRIORITY APPLN. INFO.:			CN 2002-112268	20020627
OTHER SOURCE(S):	MARPAT	142:316991		
GI				



AB Title compds. I [wherein X = R3 or OR3; Y = R4 or OR4; R1 = H or alkyl; R2 = H or NO2; R3, R4 = H, alk(en/yn)yl, hydroxyalkyl, (un)substituted aryl or heterocyclyl] were prepared. For example, 10-hydroxycamptothecin underwent acylation with iso-Bu chloroformate to give II. Some I showed 20.1-92.2% tumor inhibition at the dose of 2-6 mg/Kg, while 5-Fu showed 78.4% inhibition at a dose of 25 mg/Kg. The good antitumor activity of I is attributed to the introduction of carbonate and/or ester groups so that the active parts of camptothecins can be stabilized.

IT 19685-12-2P 848078-09-1P 848078-11-5P

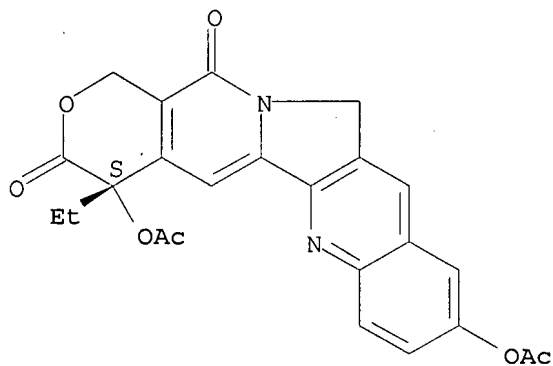
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of camptothecin carbonates and esters with enhanced antitumor activity)

RN 19685-12-2 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-4-ethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



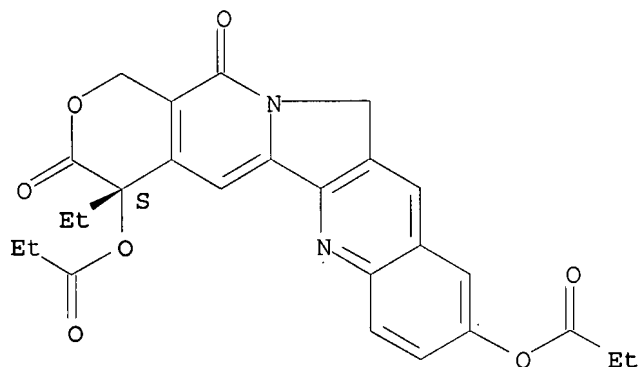
RN 848078-09-1 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4-ethyl-4,9-bis(1-oxopropoxy)-, (4S)- (CA INDEX NAME)



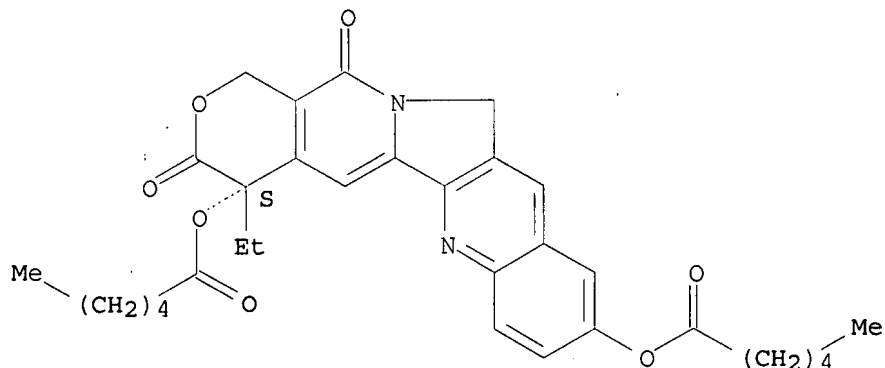
10/583,803

Absolute stereochemistry.



RN 848078-11-5 CAPLUS  
CN Hexanoic acid, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2003:795092 CAPLUS  
DOCUMENT NUMBER: 140:27961  
TITLE: Regioselective synthesis and cytotoxicities of camptothecin derivatives modified at the 7-, 10- and 20-positions  
AUTHOR(S): Pan, Xian-Dao; Han, Rui; Sun, Piao-Yang  
CORPORATE SOURCE: Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100050, Peop. Rep. China  
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(21), 3739-3741  
CODEN: BMCLE8; ISSN: 0960-894X  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 140:27961  
AB A series of 7-acyloxymethylcamptothecin and 20-O-acyl-7-acyloxymethylcamptothecin derivs. were regioselectively prepared on different solvents. 7-Acyloxymethylcamptothecins possess more efficacy than 20-O-acyl-7-acyloxymethylcamptothecins against six human cancer cell lines in vitro.

10/583,803

IT 634586-91-7P 634587-13-6P

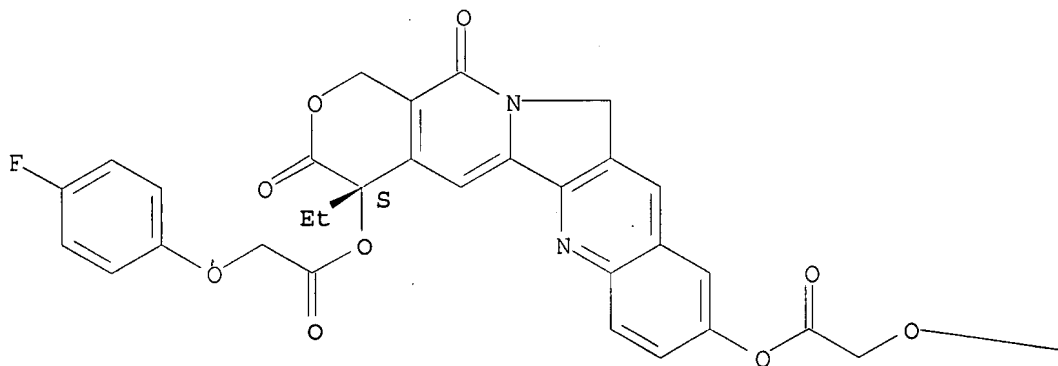
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL  
(Biological study); PREP (Preparation)  
(regioselective synthesis and cytotoxicities of camptothecin derivs.  
modified at the 7-, 10- and 20-positions)

RN 634586-91-7 CAPLUS

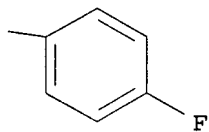
CN Acetic acid, (4-fluorophenoxy)-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-  
dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



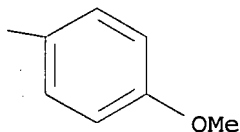
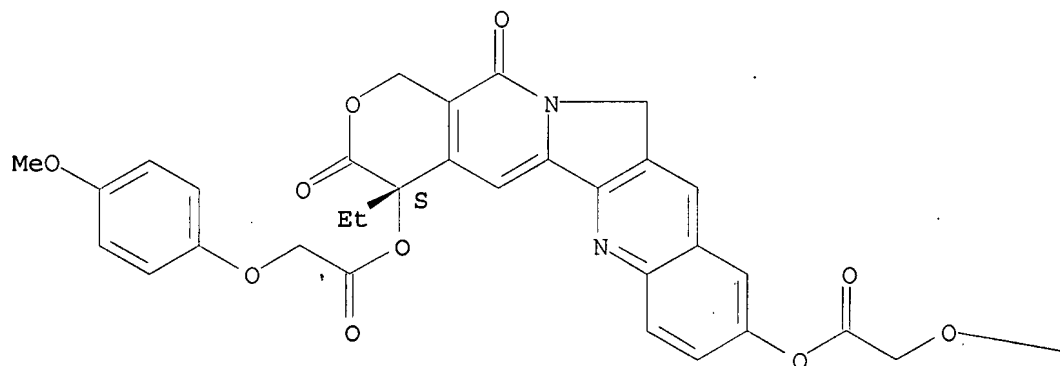
PAGE 1-B



RN 634587-13-6 CAPLUS

CN Acetic acid, (4-methoxyphenoxy)-, (4S)-4-ethyl-3,4,12,14-tetrahydro-3,14-  
dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinoline-4,9-diyl ester (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:7891 CAPLUS

DOCUMENT NUMBER: 138:354130

TITLE: Semisynthesis of DB-67 and other silatecans from camptothecin by thiol-promoted addition of silyl radicals

AUTHOR(S): Du, Wu; Kaskar, Bashir; Blumbergs, Peter; Subramanian, P.-K.; Curran, Dennis P.

CORPORATE SOURCE: Department of Chemistry, University of Pittsburgh, Pittsburgh, PA, 15260, USA

SOURCE: Bioorganic & Medicinal Chemistry (2003), 11(3), 451-458

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 138:354130

AB Thiol- or acid-promoted addns. of silyl radicals to camptothecin are reported. At 105 °C, mixts. of 7-silyl (favored) and 12-silyl

10/583,803

camptothecins are formed alongside substantial amts. of recovered camptothecin. At 160 °C, 12-silyl isomers are formed preferentially, but the total mass balance is substantially reduced. The silyl radical addition is featured in short semi-syntheses of DB-67 (7-tert-butyl dimethylsilyl-10-hydroxy camptothecin) from both camptothecin and 10-hydroxycamptothecin.

IT 19685-12-2P 521061-96-1P 521061-97-2P

521061-98-3P

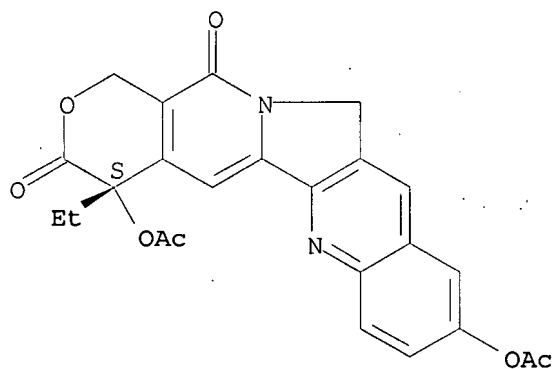
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(semisynthesis of DB-67 and other silatecans from camptothecin via the thiol-promoted addition of silyl radicals to camptothecins)

RN 19685-12-2 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-4-ethyl-, (4S)- (9CI) (CA INDEX NAME)

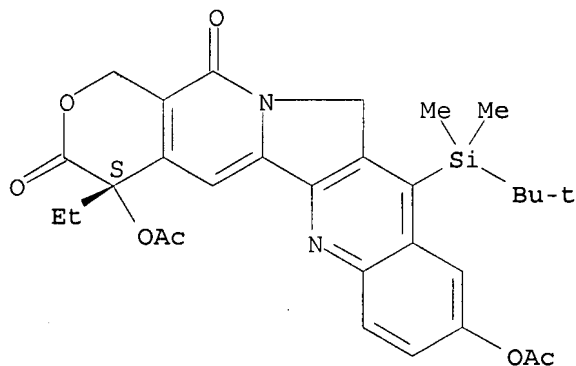
Absolute stereochemistry.



RN 521061-96-1 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-, (4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

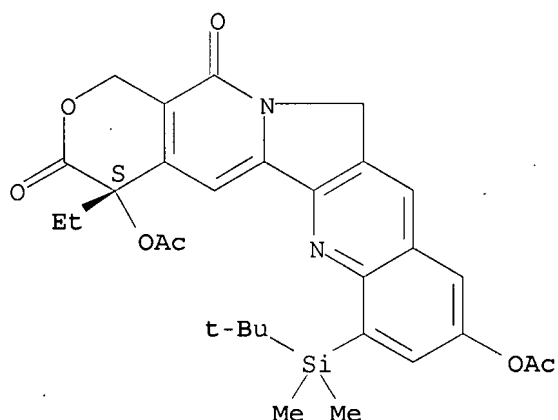


RN 521061-97-2 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione, 4,9-bis(acetyloxy)-7-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-, (4S)- (CA INDEX NAME)

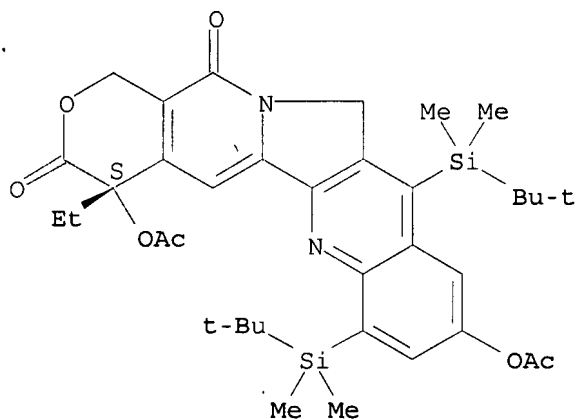
Absolute stereochemistry. Rotation (-).

10/583,803



RN 521061-98-3 CAPLUS  
CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,  
4,9-bis(acetyloxy)-7,11-bis[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-,  
(4S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:928228 CAPLUS  
DOCUMENT NUMBER: 138:4823  
TITLE: Preparation of polyglutamic acid-camptothecin conjugates  
INVENTOR(S): Bhatt, Rama; Vries, Peter; Klein, J. Peter; Tulinsky, John; Lewis, Robert A.; Singer, Jack W.  
PATENT ASSIGNEE(S): Cell Therapeutics, Inc., USA  
SOURCE: U.S. Pat. Appl. Publ., 26 pp., Cont.-in-part of U.S. Ser. No. 956,237.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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10/583,803

US 2002183243	A1	20021205	US 2002-51306	20020122
US 2002016285	A1	20020207	US 2001-810345	20010319
US 2002077290	A1	20020620	US 2001-956237	20010920
PRIORITY APPLN. INFO.:			US 2000-190429P	P 20000317
			US 2001-810345	A2 20010319
			US 2001-956237	A2 20010920

AB The invention comprises polyglutamic acid (PG)-camptothecin conjugates [PG-NH]-CH<sub>2</sub>CO-[camptothecin] [camptothecin is 20(S)-camptothecin (CPT) or a biol.-active analog] which are linked via the oxygen at position 20 of camptothecin and the  $\gamma$ -carbonyl of a monomeric unit of PG. A number of camptothecin derivs. were conjugated with polyglutamic acid and tested for antitumor activity. In general, PG-glycine conjugates of CPT were superior to PG-CPT conjugates made with other linkers and to comparable PG-glycine conjugates consisting of 20(S)-9-amino-, 20(S)-10-hydroxy-, 20(S)-7-ethyl-10-hydroxy- and 20(S)-10-acetoxy-7-(tert-butyl)dimethylsilyl)camptothecin.

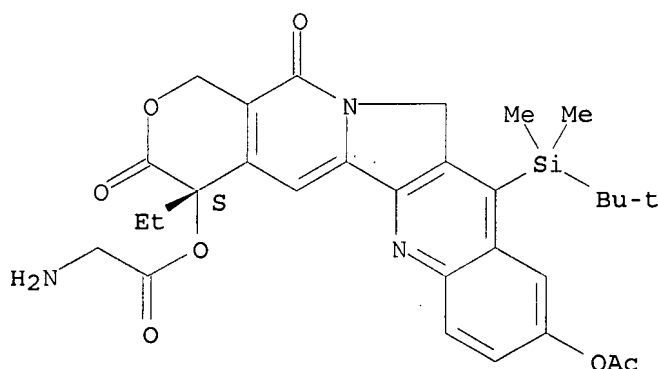
IT 362497-18-5DP, reaction products with poly(L-glutamic acid)  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and antitumor activity polyglutamic acid-camptothecin conjugates preparation and antitumor activity)

RN 362497-18-5 CAPLUS

CN Glycine, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (CA INDEX NAME)

Absolute stereochemistry.



IT 362497-17-4P 362497-19-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

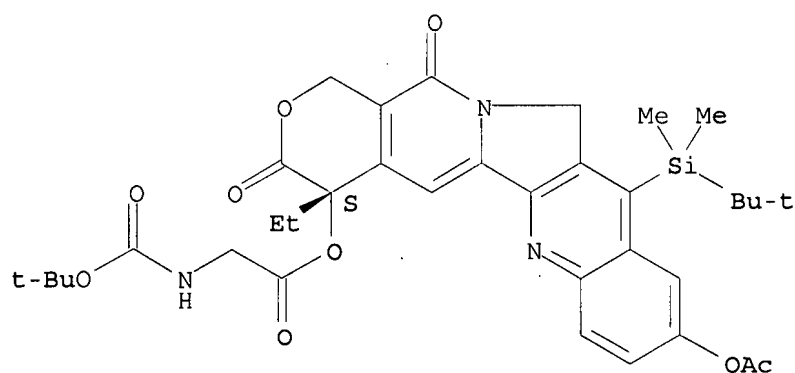
(preparation and antitumor activity polyglutamic acid-camptothecin conjugates preparation and antitumor activity)

RN 362497-17-4 CAPLUS

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (CA INDEX NAME)

Absolute stereochemistry.

10/583,803

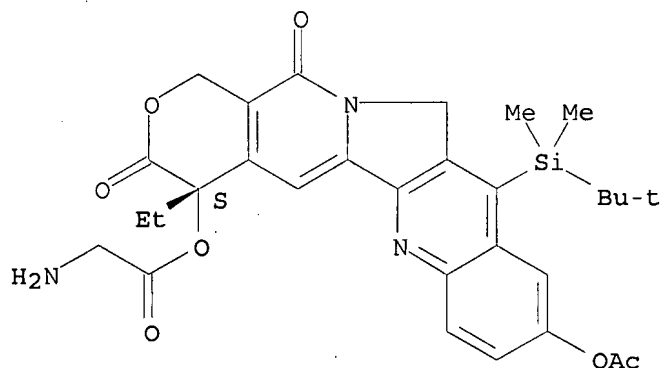


RN 362497-19-6 CAPLUS  
CN Glycine, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

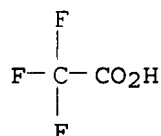
CRN 362497-18-5  
CMF C30 H35 N3 O7 Si

Absolute stereochemistry.



CM 2

CRN 76-05-1  
CMF C2 H F3 O2

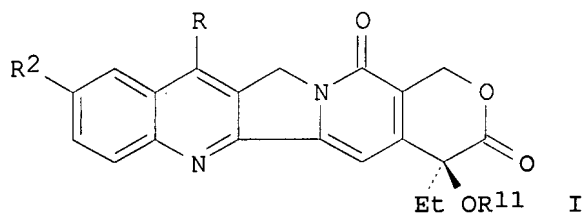


L4 ANSWER 14 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2002:615405 CAPLUS  
DOCUMENT NUMBER: 137:169684  
TITLE: Preparation and formulation of highly lipophilic camptothecin prodrugs for therapeutic use in the

10/583,803

INVENTOR(S): treatment of cancer and AIDS  
 Bom, David C.; Burke, Thomas G.  
 PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA  
 SOURCE: PCT Int. Appl., 343 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002062340	A1	20020815	WO 2002-US3548	20020206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002245394	A1	20020819	AU 2002-245394	20020206
PRIORITY APPLN. INFO.: US 2001-267040P P 20010207 WO 2002-US3548 W 20020206				
OTHER SOURCE(S): MARPAT 137:169684 GI				



AB Camptothecin amino acid ester prodrug analogs, such as I [R = -X-SiR<sub>6</sub>R<sub>7</sub>R<sub>8</sub>; X = bond or connecting alkylene, alkenylene, or alkynylene group; R<sub>2</sub> = H, OH, CN, NO<sub>2</sub>, N<sub>3</sub>, CHO, SH, halogen, alkyl, alkenyl, alkynyl, alkoxy, aryloxy, acyloxy, etc.; R<sub>6</sub>, R<sub>7</sub>, R<sub>8</sub> = alkyl, alkenyl, alkynyl, aryl, etc.; R<sub>11</sub> = CO(CH<sub>2</sub>)<sub>n</sub>NR<sub>16</sub>R<sub>17</sub>; R<sub>16</sub>, R<sub>17</sub> = H, alkyl, alkenyl, alkynyl, etc.; NR<sub>16</sub>R<sub>17</sub> = nitrogen bound heterocyclyl; n = 1-30], of highly lipophilic silatecans of potential use in the treatment of cancer and AIDS. Thus, DB 172 I [R = (CH<sub>2</sub>)<sub>2</sub>SiMe<sub>3</sub>, R<sub>2</sub> = R<sub>11</sub> = H] was O-acylated with BOC-NHCH<sub>2</sub>CO<sub>2</sub>H using DMAP in CH<sub>2</sub>Cl<sub>2</sub> to form the N-protected glycine ester I [R = (CH<sub>2</sub>)<sub>2</sub>SiMe<sub>3</sub>, R<sub>2</sub> = H, R<sub>11</sub> = COCH<sub>2</sub>NHCO<sub>2</sub>CMe<sub>3</sub>] with 48% yield. The protected glycine ester was then converted to the hydrochloride salt of I [R = (CH<sub>2</sub>)<sub>2</sub>SiMe<sub>3</sub>, R<sub>2</sub> = H, R<sub>11</sub> = COCH<sub>2</sub>NH<sub>2</sub>] with 91% yield. using HCl in dioxane. Lipophilicity, fluorescence anisotropy, and equilibrium binding consts. of the prepared camptothecin amino acid ester prodrugs were assayed.

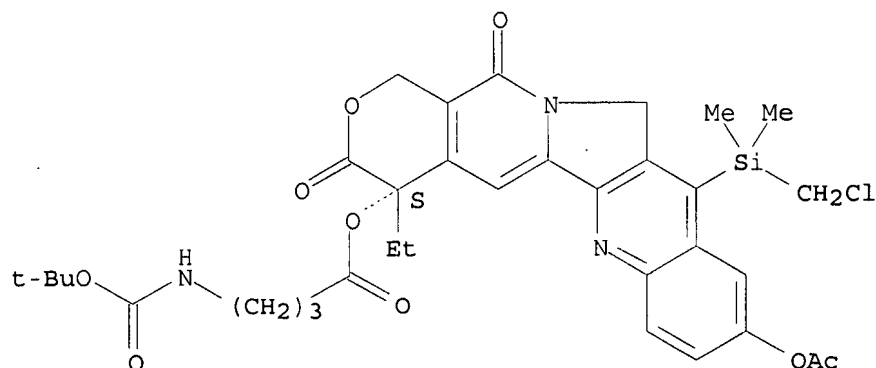
IT 446236-04-0P 446237-73-6P 446237-77-0P  
 446237-81-6P 446237-85-0P 446237-89-4P  
 446237-93-0P 446237-97-4P 446238-01-3P  
 446238-05-7P 446238-09-1P 446238-13-7P  
 446238-17-1P 446238-21-7P 446238-25-1P  
 446238-29-5P 446238-33-1P 446238-37-5P  
 446238-41-1P 446238-45-5P 446238-49-9P  
 446238-53-5P 446238-57-9P 446238-61-5P  
 446238-65-9P 446238-69-3P 446238-73-9P



10/583,803

CN Butanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]-, (4S)-9-(acetyloxy)-11-[(chloromethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:466699 CAPLUS

DOCUMENT NUMBER: 137:28287

TITLE: Polyglutamic acid-camptothecin conjugates and methods of preparation

INVENTOR(S): Bhatt, Rama; De Vries, Peter; Klein, J. Peter; Tulinsky, John; Lewis, Robert A.; Singer, Jack W.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U. S. Ser. No. 810,345.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002077290	A1	20020620	US 2001-956237	20010920
US 2002016285	A1	20020207	US 2001-810345	20010319
US 2002183243	A1	20021205	US 2002-51306	20020122
US 2003211973	A1	20031113	US 2003-407218	20030407
US 7153864	B2	20061226		
US 2003216289	A1	20031120	US 2003-407217	20030407
US 7173041	B2	20070206		

PRIORITY APPLN. INFO.:  
US 2000-190429P P 20000317  
US 2001-810345 A2 20010319  
US 2001-956237 A2 20010920

AB The invention provides polyglutamic acid-camptothecin conjugates and methods for their preparation and use. A number of camptothecin derivs. were conjugated with polyglutamic acid and tested for antitumor activity.

IT 362497-19-6DP, reaction products with poly(L-glutamic acid)  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polyglutamic acid-camptothecin conjugates preparation and antitumor activity)

RN 362497-19-6 CAPLUS

10/583,803

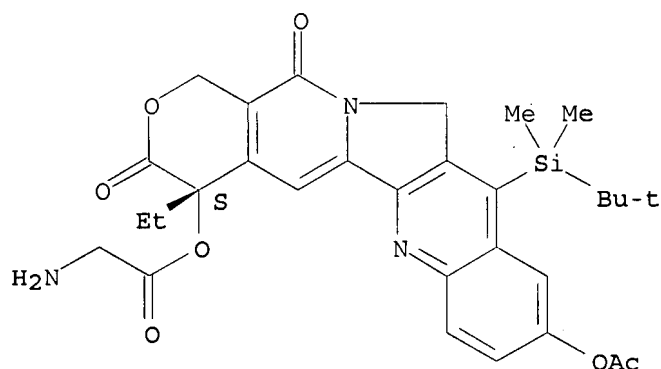
CN Glycine, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 362497-18-5

CMF C30 H35 N3 O7 Si

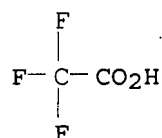
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



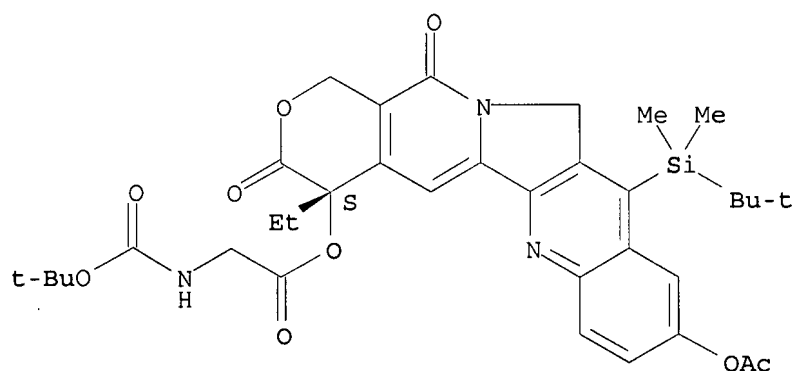
IT 362497-17-4P 362497-19-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(polyglutamic acid-camptothecin conjugates preparation and antitumor activity)

RN 362497-17-4 CAPLUS

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (CA INDEX NAME)

Absolute stereochemistry.

10/583,803



RN 362497-19-6 CAPLUS

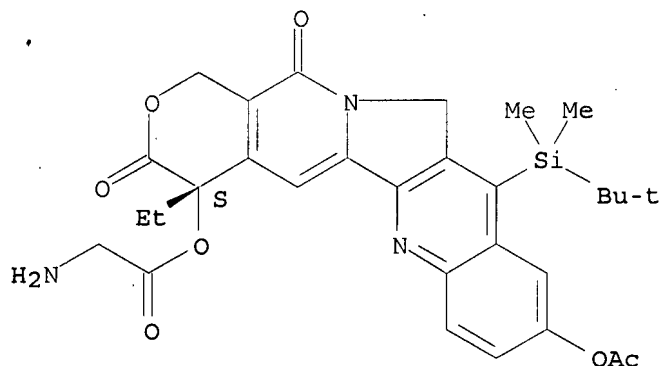
CN Glycine, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 362497-18-5

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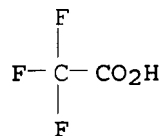
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L4 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:713182 CAPLUS

DOCUMENT NUMBER: 135:262261

TITLE: Preparation and antitumor activity of polyglutamic acid-camptothecin conjugates

INVENTOR(S): Bhatt, Rama; De Vries, Peter; Klein, J. Peter; Lewis, Robert A.; Singer, Jack W.; Tulinsky, John  
 PATENT ASSIGNEE(S): Cell Therapeutics, Inc., USA  
 SOURCE: PCT Int. Appl., 81 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001070275	A2	20010927	WO 2001-US8553	20010319
WO 2001070275	A3	20020103		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2402643	A1	20010927	CA 2001-2402643	20010319
AU 200147513	A	20011003	AU 2001-47513	20010319
EP 1267939	A2	20030102	EP 2001-920466	20010319
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
HU 2002004562	A2	20030428	HU 2002-4562	20010319
JP 2003527443	T	20030916	JP 2001-568471	20010319
SI 21172	A	20031031	SI 2001-20021	20010319
BR 2001009272	A	20040629	BR 2001-9272	20010319
IN 2002KN01144	A	20050311	IN 2002-KN1144	20020910
NO 2002004421	A	20021115	NO 2002-4421	20020916
ZA 2002007423	A	20031217	ZA 2002-7423	20020916
MX 2002PA09082	A	20031211	MX 2002-PA9082	20020917
PRIORITY APPLN. INFO.:			US 2000-190429P	P 20000317
			WO 2001-US8553	W 20010319

OTHER SOURCE(S): MARPAT 135:262261

AB Methods for the preparation of polyglutamic acid-therapeutic agent conjugates are disclosed. The compds. show antitumor activity. Thus, 20(S)-camptothecin was allowed to react with N-(tert-butoxycarbonyl)glycine in DMF solution in the presence of 4-dimethylaminopyridine followed by the addition of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide. The product, 20-O-(N-(tert-butoxycarbonyl)glycyl)camptothecin, was deprotected with CF<sub>3</sub>CO<sub>2</sub>H to give 20-O-(glycyl)camptothecin trifluoroacetic acid salt which was then treated with poly-(L-glutamic acid). The conjugate, polyglutamate-glycine-camptothecin showed high antitumor activity.

IT 362497-17-4P 362497-19-6P

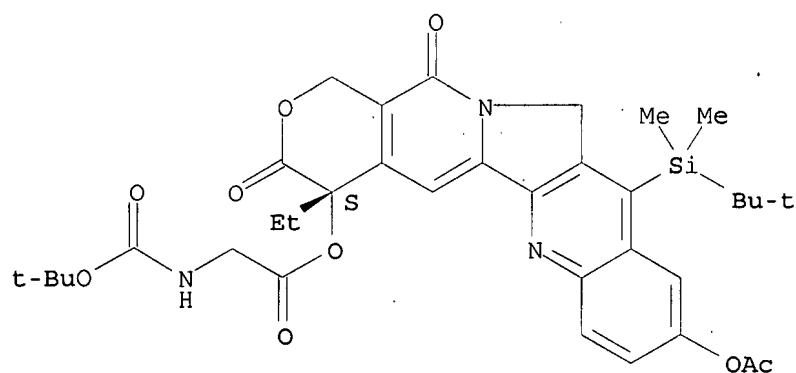
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation and antitumor activity of polyglutamic acid-camptothecin conjugates)

RN 362497-17-4 CAPLUS

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester (CA INDEX NAME)

Absolute stereochemistry.

10/583,803



RN 362497-19-6 . CAPLUS

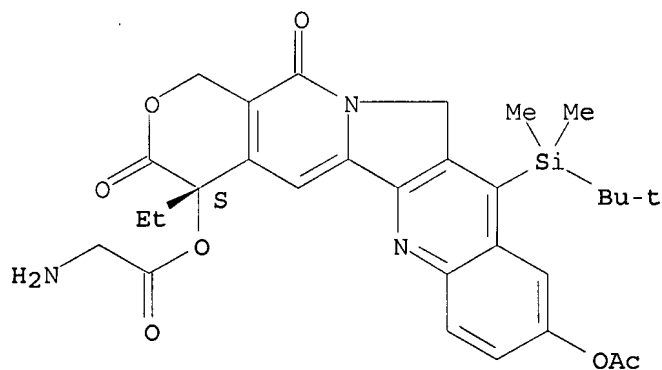
CN Glycine, (4S)-9-(acetyloxy)-11-[(1,1-dimethylethyl)dimethylsilyl]-4-ethyl-3,4,12,14-tetrahydro-3,14-dioxo-1H-pyrano[3',4':6,7]indolizino[1,2-b]quinolin-4-yl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 362497-18-5

CMF C30 H35 N3 O7 Si

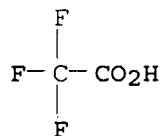
Absolute stereochemistry.



CM 2

CRN 76-05-1

CMF C2 H F3 O2



L4 ANSWER 17 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1969:422230 CAPLUS

DOCUMENT NUMBER: 71:22230

ORIGINAL REFERENCE NO.: 71:4109a,4112a

TITLE: Plant antitumor agents. II. Structure of two new

10/583,803

alkaloids from *Camptotheca acuminata*  
AUTHOR(S): Wani, Mansukhlal C.; Wall, Monroe E.  
CORPORATE SOURCE: Res. Triangle Inst., Durham, NC, USA  
SOURCE: Journal of Organic Chemistry (1969), 34(5), 1364-7  
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal  
LANGUAGE: English

GI For diagram(s), see printed CA Issue.

AB Fractionation of *C. acuminata* yielded 2 new alkaloids hydroxycamptothecin (I) and methoxycamptothecin (II). I could be methylated to give a Me ether identical with II. In order to establish the position of the OH group in ring A, N.M.R. spectra of deuterated II and of model compds. were obtained. The syntheses of the model compds. were described.

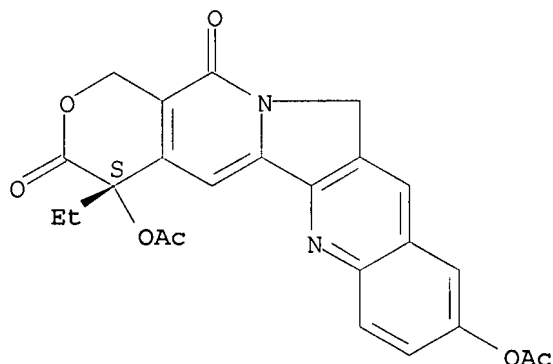
IT 19685-12-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

RN 19685-12-2 CAPLUS

CN 1H-Pyrano[3',4':6,7]indolizino[1,2-b]quinoline-3,14(4H,12H)-dione,  
4,9-bis(acetyloxy)-4-ethyl-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 17:04:34 ON 15 NOV 2007)

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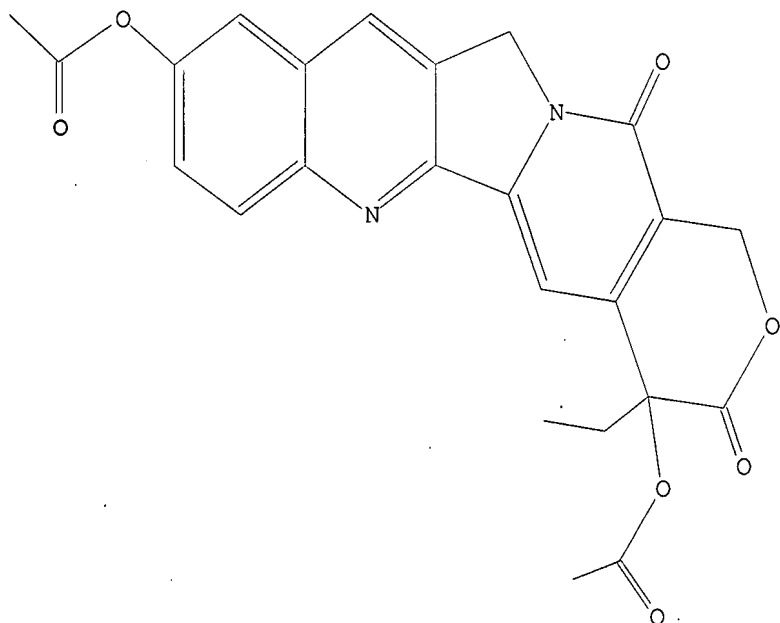
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L1 HAS NO ANSWERS

L1 STR

10/583,803



Structure attributes must be viewed using STN Express query preparation.

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